PATENT

Attorney Docket No.: ROCH-001DIV
(R0058C-DIV)

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the U.S. Postal Service as first class mail in an envelope addressed to:
Mail Stop: Board of Patent Appeals and Interference, US Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450, on the date indicated below.
Name of Person Mailing:

Signature: _____
Date: 10/12/04

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re application of:

Paul David Cannon et al.

Application No.: 10/052,664

Filed: January 17, 2002

For: HUMAN INTESTINAL NPT2B

Assignee: Roche Palo Alto LLC

Examiner: Nirmal Singh Basi

Technology Unit: 1600

Art Unit: 1646

Appeal Brief

Board of Patent Appeals and Interference
Alexandria, VA 22313-1450

APPEAL BRIEF (37 CFR §1.192)

This is an appeal from the Final Rejection in the Office Action mailed May 19, 2004, by the U.S. Patent and Trademark Office (USPTO) in the above referenced patent application. A Notice of Appeal was timely filed on July 12, 2004. Jurisdiction over this Appeal resides in the Board of Patent Appeals and Interferences (the Board) under 35 USC § 134. Applicants reserve the right to request an oral hearing.

I. Real Party in interest

Roche Palo Alto LLC, the assignee of the above referenced patent application is the real party in interest.

II. Related appeals and interferences

There are no related appeals or interferences.

III. Status of Claims

Claim 1 is pending in this application. Claim 1 has been rejected under 35 USC § 101 and 35 USC § 112, first paragraph. The rejection of Claim 1 is appealed.

IV. Status of Amendments

No amendments have been filed subsequent to final rejection.

V. Summary of the Invention

The presently claimed invention relates to a polypeptide composition for a novel human sodium phosphate co-transporter, designated as Npt2B, expressed in intestinal epithelial cells (stated on page 4 lines 9-10 in Substitute Specification filed on April 30, 2002). Using the procedures disclosed in Experimental section A (page 28 line 24 to page 29 line 21), the Npt2B polypeptide was determined to have the amino acid sequence shown in Fig. 1 and identified as SEQ ID NO:1 (stated on page 5 line 5). A description of the function of Npt2B appears on page 4 lines 19-24 in the Substitute Specification:

> Npt2B is a type II sodium phosphate co-transporter. In its native environment, Npt2B is a co-transporter of sodium cation and phosphate anion. Npt2B is expressed, among other locations, on the surface of intestinal epithelial cells, i.e. on the apical or intestinal luminal side of the epithelial cells, and therefore provides for the transport of sodium and phosphate ions from the intestinal lumen into the intestinal epithelial cells.

The function of the Npt2B polypeptide as a human intestinal sodium phosphate co-transporter was derived both from the homology to published sequences for the type II intestinal transporters from *Xenopus* and mouse (page 29, lines 15-21 and references cited therein, Ishizuya-Oka et al., *Development Genetics* 20:53-66, 1997; Hilfiker et al., *Proc. Natl. Acad. Sci. U.S.A.* 95:14564-14569, 1998) **and** from the expression of the Npt2B cDNA in mammalian cells and assaying for sodium-phosphate transporter activity as described in Experimental section B (page 29 line 23 to page 30 line 19). To date, Npt2B is the sole type II human sodium phosphate co-transporter known that is found in the intestine (see Xu et al., *Biochim Biophys Acta* 1567:97-105, 2002; Werner & Kinne, *J Physiol Regul Integr Comp Physiol* 280(2):R301-312, 2001; both references cited in the Amendment and Response submitted by Applicants/Appellants on February 23, 2004).

Descriptions of the utilities of the claimed invention appear throughout the specification, and are stated, for example, on page 9 lines 28-30 as: "[t]he subject polypeptide and nucleic acid compositions find use in a variety of different applications, including research, diagnostic, and therapeutic agent screening/discovery/preparation applications, as well as in therapeutic compositions and methods employing the same." One specific utility is its use in various screening assays designed to identify therapeutic agents. As stated in the specification on page 17 lines 9-21:

> The subject Npt2B polypeptides find use in various screening assays designed to identify therapeutic agents. Thus, one can use a cell model such as a host cell, e.g. CHO, HEK293, COS7, Xenopus Oocyte, etc., which has been transfected in a manner sufficient to express Npt2B on its surface. One can then contact the cell with a medium comprising sodium and phosphate ions, and measure the amount of phosphate anions that are internalized in the cell, where measurements are taken in both control environments and test environments, e.g. in the presence of a candidate Npt2B modulator compound, e.g. an Npt2B agonist or an Npt2B antagonist or inhibitor. To assist in detection of Pi uptake, labeled phosphorous is present in the medium, where any convenient label may be employed, such as an isotopic label, e.g. as present in ^{32}P or ^{33}P. Alternatively, current measurements may be taking using well known electrophysiological methods (see e.g. Electrophysiology, A practical Approach (IRL Press)(1993)), from which the

> uptake of Pi may be determined. Examples of assays for measuring Pi uptake are provided in: Maganin et al., *Proc. Nat'l Acad. Sci USA* (July 1993) 90: 5979-5983; and Helps et al., *Eur. J. Biochem.* (1995) 228: 927-930..

Another example of an Npt2B modulatory agent would be "antibodies that at least reduce, if not inhibit the target Npt2B activity in the host. Suitable antibodies are obtained by immunizing a host animal with peptides *comprising all or a portion of the target protein, e.g. Npt2B* [emphasis added]" (page 21 lines 3-5).

The significance of identifying Npt2B modulatory agents or compounds, which either increase Npt2B activity (i.e. enhances intestinal phosphate absorption), or reduce or inhibit Npt2B activity (i.e. stops or limits intestinal phosphate absorption) appears on page 27, lines 19-29, and is as follows:

> The subject methods [of modulating Npt2B activity] find use in the treatment of a variety of different disease conditions involving Npt2B activity. As such, the disease conditions treatable according to the subject methods include diseases characterized by abnormally high Pi absorption and disease conditions characterized by abnormally low Pi absorption. Disease conditions resulting from abnormally low Npt2B activity are those characterized by the presence of hypophosphatemia, and include: osteomalacia, hypocalciurea, rickets, and the like. Disease conditions resulting from abnormally high Npt2B activity are those characterized by the presence of hyperphosphatemia and include: hyperparathyroidism, hypocalcemia, vitamin D deficiency, soft tissue or metastic calcification, and the like. Of particular interest is the use of the subject methods to treat hyperphosphatemia resulting from renal insufficiency, e.g. caused by renal disease resulting in at least impaired renal function, and the like.

Therefore, use of the Npt2B polypeptide to identify modulatory agents that increase Npt2B activity (i.e. increase intestinal phosphate absorption) would be therapeutically desirable for the treatment of diseases resulting from hypophosphatemia. Conversely, use of the Npt2B polypeptide to identify or prepare modulatory agents that decrease Npt2B activity (i.e. decrease intestinal phosphate absorption) would be therapeutically desirable for the treatment of diseases resulting from hyperphosphatemia.

VI. Issues

A. Whether the invention as defined by Claim 1 is patentable under 35 USC § 101 because it has a specific and substantial utility or a well-established utility; and

B. Whether the specification enables Claim 1 under 35 USC § 112, first paragraph, since the invention is supported by a specific and substantial asserted utility or a well-established utility.

VII. Grouping of Claims

This appeal concerns the rejection of Claim 1 only, the sole pending claim.

VIII. Argument

A1. Utility under 35 USC § 101

In the Office Action dated November 20, 2003 (OA 11/20/03), the Examiner rejected claim 1 under 35 USC § 101 as allegedly being not supported by either a specific and substantial asserted utility or a well-established utility. The Examiner did not discuss the credibility of the utility asserted in the specification, which implies that the asserted utility of the invention was considered credible by the Examiner. The rejection of claim 1 under 35 USC § 101 was maintained in the Final Office Action dated May 19, 2004 (OA 5/19/04).

B1. Standard of Rejection under 35 USC § 101

To properly reject a claimed invention under 35 USC § 101, the Examiner bears the burden of establishing a *prima facie* showing that the claimed invention lacks patentable utility, and needs to provide a sufficient evidentiary basis for factual assumptions relied upon in establishing the *prima facie* showing. If this initial burden is met, then burden shifts to the applicant of the claimed invention to provide evidence or argument to rebut the *prima facie* showing. Therefore, compliance with 35 USC § 101 is a question of fact.

Raytheon v. Roper, 724 F.2d 951, 956, 220 USPQ 592, 596 (Fed. Cir. 1983). Cases addressing the standard of rejection under 35 USC § 101 include:

In re Gaubert, 524 F.2d 1222, 1114, 187 USPQ 664, 666 (CCPA 1975) ("Accordingly, the PTO must do more than merely question operability – it must set forth factual reasons which would lead one skilled in the art to question the objective truth of the statement of operability.")

In re Oetiker, 977, F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992) ("[T]he examiner bears the initial burden, on review of the prior art or on any other ground, of presenting a *prima facie* case of unpatentability. If that burden is met, the burden of coming forward with evidence or argument shifts to the applicant ... After evidence or argument is submitted by the applicant in response, patentability is determined on the totality of the record, by a preponderance of evidence with due consideration to persuasiveness of argument ... If examination at the initial stage does not produce a *prima facie* case of unpatentability, then without more the applicant is entitled to grant of the patent.")

In re Brana, 51 F.3d 1560, 1566, 34 USPQ2d 1436, 1441 (Fed. Cir. 1995) ("Only after the PTO provides evidence showing that one of ordinary skill in the art would reasonably doubt the asserted utility does the burden shift to the applicant to provide rebuttal evidence sufficient to convince such a person of the invention's asserted utility.")

C1. Application of Standard of Rejection under 35 USC § 101 to Claim 1

Applicants/Appellants submit that the Examiner has not met the burden of presenting a *prima facie* case that the claimed invention lacks patentable utility by providing evidence showing that one of ordinary skill in the art would reasonably doubt the utility asserted in the specification.

As previously stated in the Summary of the Invention (Section V) and briefly restated here, the specification discloses a specific function for the claimed invention, which is a human type II sodium phosphate co-transporter that provides for the transport of sodium and phosphate ions from the intestinal lumen into the intestinal epithelial cells (page 4 lines 9 and 19-24). This is a unique function for Npt2B since no other type II human intestinal sodium phosphate co-transporter have been identified (see Xu et al., *Biochim Biophys Acta* 1567:97-105, 2002; Werner & Kinne, *J Physiol Regul Integr Comp Physiol* 280(2):R301-312, 2001). That this statement is true even today can been seen in the most current review on Type II sodium phosphate co-transporters by Murer et al., *Pflugers Arch.* 447(5):763-767, 2004 (attached herein as "Exhibit A"). Based on this unique and specific function of Npt2B, the specification discloses several specific utilities for the claimed invention. One example of a specific utility for the Npt2B polypeptide is its "use in various screening assays designed to identify therapeutic agents [that modulate Npt2B activity]." (page 17 lines 9-10). Another disclosed specific utility for the Npt2B polypeptide is its use as an immunogen to generate antibodies that reduce or inhibit Npt2B activity in a subject. (page 21 lines 3-5). Still another specific utility is the use of the Npt2B protein or protein fragments "as therapeutic agents in situations where one wishes to enhance Npt2B activity in a host, e.g. disease conditions associate[d] with hypophosphatemia" and in "gene therapy to treat disorders associated with Npt2B defects." (page 19, lines 9-12). Specific diseases that are treatable by modulating Npt2B activity, either by modulatory compounds, antibodies, or gene therapy are disclosed in the specification on page 27 lines 19-29, and were previously stated in the Summary of Invention.

The asserted utilities of the claimed Npt2B polypeptide are "substantial" or "practical" utilities, which the Courts have defined as follows, "Practical utility is a shorthand way of attributing "real-world" value to claimed subject matter. In other words, one skilled in the art can use a claimed discovery in a manner which provides some immediate benefit to the public." in *Nelson v. Bowler*, 626 F.2d 853,856, 206 USPQ 881, 883 (CCPA 1980).

The term "immediate benefit to the public" does not mean that products or services based on the claimed invention must be currently available to the public, but rather that the invention contains the characteristics "where specific benefit exists in currently available form." See *Brenner v. Manson*, 383 U.S. 519, 534-35, 148 USPQ 689, 695 (1966) and MPEP 2107.01.

In the present case, by following the procedures described in Experimental section B of the specification (page 29 line 23 to page 30 line 19), the Npt2B polypeptide can be used in a screening assay to identify therapeutic agents that modulate Npt2B activity (page 17, lines 9-10).[1] Also, by examining the amino acid sequence of Npt2B disclosed in SEQ ID NO:1, the claimed polypeptide can be used as an immunogen to generate antibodies that reduce or inhibit Npt2B activity (page 21 lines 3-5). In both situations, the claimed Npt2B polypeptide, in its available form at the time of filing, is able to provide benefit to the public by identifying modulatory agents for the treatment of diseases associated with high Npt2B activity, i.e. hyperphosphatemia or with low Npt2B activity, i.e. hypophosphatemia (for list of diseases, see page 27 lines 19-29).

In neither OA 11/20/03 nor OA 5/19/04 does the Examiner provide any evidence or *factual* reasons why one skilled in the art would reasonably doubt the asserted specific and substantial utilities of the claimed Npt2B polypeptide. In fact many of the "reasons" provided by the Examiner in raising and maintaining the 35 USC § 101 rejection are contrary both to specific statements in the specification and to knowledge in the field of the art either at the time of filing or at present.

[1] It should be noted that the use of a protein as a screening target is a use with immediate commercial importance. For example, Chiron's 2003 annual report disclosed that it received US$4.0 million from Boehringer Ingelheim in exchange for a **non-exclusive** license to screen against HCV drug targets. ("*Boehringer Ingelheim*: In December 2003, we granted Boehringer Ingelheim a nonexclusive license for the research, development and commercialization of small molecule therapeutics against hepatitis C virus drug targets. We recognized $4.0 million in 2003 under this arrangement." Chiron 2003 Annual Report at p. 47) Applicants do not assert that their invention will

Examples of statements contrary to the specification can be found in OA 11/20/03, page 4 line 21 to page 5 line 5: "There is no disclosure provided within the instant specification on what specific function the protein of SEQ ID NO:1 possess, or how to specifically assay for such, ligands that bind, promoters that activate; nor are any cell type/tissues disclosed that specifically nor are any disease states disclosed that are directly related to said protein dysfunction. The specification fails to disclose, what disease is associated with claimed sodium phosphate co-transporter dysfunction or what drugs affect specific claimed sodium phosphate co-transporter function."; and also in OA 5/19/04, page 3 line 21 to page 4 line 2: "the specification does not disclose what claimed sodium phosphate co-transporter specifically regulates and what specific disease, claimed sodium phosphate co-transporter, is a target for. The specification provides a diverse list of disease states that may be involved in Pi dysfunction."

These contentions are in direct contradiction to clear statements in the specification in which the specific function of the claimed Npt2B polypeptide (page 4, lines 9-10; 19-24) as well as specific diseases associated with the Npt2B polypeptide (page 27, lines 19-29) were disclosed, thereby setting forth specific and substantial asserted utilities for the claimed invention. The Examiner cannot attempt to establish a showing that the claimed invention lacks patentable utility simply by *ignoring statements that assert the specific function and utility of the invention*, and then declaring that the specification fails to disclose any specific function or utility of the invention.

There are also numerous statements made by the Examiner which have no factual support in the knowledge in the field of Type II sodium phosphate cotransporters, either at the time of filing or currently. Examples of such statements are as follows:

---

garner similar amounts in royalties or licensing fees: only that the rights to screen a particular protein target in search of therapeutic drugs is a valuable and immediately commercializable right and utility.

"Members of sodium phosphate co-transporter family are also highly divergent in their effects and ligand specificity. The outcome of the cellular signaling effect varies depending on the specific sodium phosphate co-transporter and the substrate activating said co-transporter." (OA 11/20/93 page 3 line 23 to page 4 line 4).

"The utility of claimed sodium phosphate co-transporter cannot be implicated solely from homology to known sodium phosphate co-transporter or their protein domains because the art does not provide teaching stating that all members of family of sodium phosphate co-transporter must have the same effects, the same ligands, and be involved in the same disease states, *the art discloses evidence to the contrary* [emphasis added] (see above)" (OA 11/20/93 page 6 lines 18-23).

"Therefore, references discussed above disclose the unpredictability of assigning a function to a particular protein based on homology, *especially one that belongs to the family sodium phosphate co-transporter which have very different ligand specificity and functions* [emphasis added]." (OA 11/20/93 page 8 line 21 to page 9 line 2).

"All members of the sodium phosphate co-transporter family have a utility in selectively screening of candidate drugs that target sodium phosphate co-transporter." (OA 11/20/93 page 9 lines 5-7).

"Further, sodium phosphate co-transporter family to which the polypeptide of SEQ ID NO:1 belongs is a family in which the members have *divergent functions* based on which tissues the protein is expressed or administered to. Assignment to this family does not support an inference of utility because the members are not known to share a common utility." (OA 11/20/93 page 11 lines 17-21, emphasis added).

"The members of the [sodium phosphate co-transporter] family have different biological activities which may be related to tissue distribution but there is no evidence that the claimed compounds share any one of diverse number of activities." (OA 11/20/93 page 12 lines 8-11).

"It is also not clear how the claimed polypeptide can be specific for both disease states that are characterized by abnormally high phosphate absorption as well as abnormally low phosphate absorption." (OA 5/19/04 page 5 lines 10-12).

> "Further, the person of ordinary skill in the art would not find substantial the assertion that just because a polypeptide transports phosphate automatically means it has to be involved in any of the diseases claimed by Applicant based on the disclosure." (OA 5/19 page 5 lines 19-21; *Note: here the Examiner acknowledges that diseases are disclosed but argues that the artisan would not find a substantial utility for the invention*).

The general knowledge in the area of Type II sodium phosphate cotransporters, especially the Type IIb intestinal transporter (i.e. Npt2B which is also referred as NaPi-IIb) at the time of filing of the priority application, February 9, 1999, can be ascertained from three references. Hilfiker et al (*Proc. Natl. Acad. Sci. U.S.A.* 95:14564-14569, 1998, cited in the specification on page 2 lines17-18 and page 29 lines 20-21) describes the cloning and characterization of mouse Npt2B with a protein sequence which has 78.8% sequence identity to the amino acid sequence of the claimed invention. Feild et al. and Xu et al. (*Biochem. Biophys. Res. Comm.* 258:578-582, 1999; *Genomics* 62:281-284, 1999; cited by Applicants/Appellants in the Supplemental Information Disclosure Statement sent to the USPTO on May 23, 2003) describe the cloning and characterization of human Npt2B/NaPi-IIb which show, respectively, 99.7% and 99.9% sequence identity to the Npt2B polypeptide sequence of the claimed invention. Although Feild et al. (May, 1999) and Xu et al. (December, 1999) were published three months and ten months after Applicants' priority date (and therefore cannot anticipate or render obvious the claimed invention), they evidence the knowledge possessed by one skilled in the art at about the time of filing. All three references clearly described their cloned product as the intestinal sodium-phosphate cotransporter, supported by functional activity showing phosphate transport. The significance attributed by the authors of these papers to their findings can be represented by these statements in the Abstract by Xu et al.:

> "Phosphate plays a crucial role in cellular metabolism and its homeostatic regulation in intestinal and renal epithelial is critical. Apically expressed sodium-phosphate (Na^+-Pi) transporters play a ***critical*** role in this regulation. We have isolated a cDNA (HGMW-approved symbol SLC34A2) encoding a novel human small intestinal Na^+-Pi transporter." (emphasis added)

Therefore, in contrast to the Examiner's statements, a person of ordinary skill in the art would, at the time of filing, immediately appreciate why the claimed Npt2B polypeptide is useful based on the characteristics of the invention. Applicants/Appellants also submit that based on the evidence presented concerning the knowledge possessed by one skilled in the art at the time of filing, the asserted specific and substantial utility for the claimed invention also qualifies as a well-established utility.

Current knowledge in the area of Type IIb intestinal sodium phosphate transporters also fully contradict the Examiner's assertions that the claimed Npt2B polypeptide has no specific or substantial utility (for the most current review on Type IIb sodium phosphate cotransporters, see Murer et al., *Pflugers Arch.* 447(5):763-767, 2004). A recent article by Peerce et al. (*Biochem. Biophys. Res. Commun.* 301:8-12, 2003) cited in the Declaration of Suryanarayna Sankuratri (submitted by Applicants/Appellants on February 23, 2004 and discussed in greater detail below) states, "[a] pharmacological method of reducing intestinal phosphate absorption may provide a more palatable approach to reducing serum phosphate and may slow the progression of moderate chronic renal failure to end-stage renal failure. In the proximal small intestine phosphate absorption occurs by a Na^+-dependent mechanism ... [which] occurs through the Na^+/phosphate cotransporter. The Na^+/phosphate cotransporter has been identified as a 110-120kDa polypeptide [references including Hilfiker et al. and Xu et al.]." This statement in Peerce et al. supports and confirms the disclosure in the specification on page 27 lines 27-29 which reads, "[o]f particular interest is the use of the subject methods [of modulating Npt2B activity] to treat hyperphosphatemia resulting from renal insufficiency, e.g. caused by renal disease resulting in at least impaired renal function, and the like."

In OA 11/20/03, the Examiner sought to support the rejection under 35 USC § 101 by implying that the disclosure in the present specification was analogous to the situations decided by the Courts in *Brenner v Manson*, 383 U.S. 519, 148 USPQ 689 (1966) (page

11 lines 12-14; page 14 lines 7-12) and in *In re Kirk*, 376 F.2d 936, 153 USPQ 48 (CCPA 1967) (page 14 line 21 to page 15 line 7). These analogies are fallacious for the following reasons. In *Brenner*, the applicant failed to disclose **any** utility for a process to synthesize a steroid compound with no known utility, other than as a possible object of scientific inquiry, and offered as evidence only a third party article showing the utility of an homologue of the subject steroid compound. In *Kirk*, the applicants claimed steroid compounds said to have valuable "biological properties" and to be of value to the furtherance of steroidal research. In contrast, the present specification discloses a specific function of the Npt2B polypeptide and its use to identify agents to treat specific diseases. Furthermore, the specification asserts both specific and substantial utilities for the Npt2B polypeptide that are supported by both the prior art and present knowledge in the field.

In responding to the utility rejection posed by the Examiner in OA 11/20/93, Applicants/ Appellants submitted the Declaration under 37 CFR §1.132 by Dr. Suryanarayana Sankuratri (filed on February 23, 2004), which contained figures and data showing functional characteristics of the claimed Npt2B polypeptide *derived by following the procedure disclosed in the specification, Experimental section B* (page 29 line 23 to page 30 line 19). The attached Figure 6 in the Declaration demonstrated that the asserted utility in the specification of identifying therapeutic agents that modulate Npt2B activity was achieved by the identification of several inhibitors of Npt2B. In OA 5/19/04, the Examiner sought to disparage the evidence presented in the Declaration on the specific and substantial utility of the claimed Npt2B polypeptide by stating in page 4 lines 15-21:

> "It is noted, at the time of filing of instant Patent Application, the claimed polypeptide *was not expressed in a cell* to determine its transport properties, or even to specifically show it transports sodium or phosphate. The sodium dependence of claimed polypeptide was unknown. In instant case *post filing art cannot be used to establish utility* because the results of said art were not known at the time of filing of instant application, and the information obtained was due to further experimentation." [emphasis added]

Applicants/Appellants submit that these statements by the Examiner are incorrect both in fact and in law. The declarant followed the procedures set forth in the Specification, and without more, confirmed the activity that was disclosed in the Specification. This demonstrates and proves that the Specification was enabling as of the filing date. The data in the Declaration served to *confirm* the specific function and at least one specific utility (use in screening assays to identify modulatory agents) of the claimed invention *which had already been asserted in the specification*. Even if the Examiner was correct in assuming that the Npt2B polypeptide had not yet been expressed in a cell at the time of filing, this does not negate the specific and substantial utility of using Npt2B as an immunogen to generate antibodies that are used to treat specific diseases of phosphate metabolism. Second, how can the Examiner conclude that the sodium dependence of Npt2B was unknown at the time of filing when the specification consistently refers to the claimed invention as a *sodium* phosphate co-transporter, which is reflected even in the **name** of this protein, *N*pt2B (*Na* Pi transporter 2B)?

Third, the Examiner states that post filing art cannot be used to establish utility. This is contrary to law. The data presented in the Declaration were not used to *identify* a utility but to *substantiate* utility already asserted in the specification. *In re Brana, supra* is directly on point:

> "The Kluge declaration, though dated after applicants' filing date, can be used to substantiate any doubts as to the asserted utility since this pertains to the accuracy of a statement already in the specification. *In re Marzocchi*, 439 F.2d at 224 n.4, 169 USPQ at 370 n.4. It does not render an insufficient disclosure enabling, **but instead goes to prove that the disclosure was in fact enabling when filed** (i.e. demonstrated utility)." (34 USPQ2d at 1441, emphasis added.)

In summary, Applicants identified and sequenced Npt2B, and set forth several utilities in the specification, including the use in screening assays and the use to generate antibodies. These utilities are unique to Npt2B, as it is the only sodium-phosphate co-transporter

found in the human intestine, and therefore mediates all absorption of phosphate from the diet. Even the Examiner found that the sodium-phosphate transporter family was diverse, and that one would not expect compounds that affect one transporter to modulate another.[2] The Declaration of Suryanarayna Sankuratri submitted by Applicants/Appellants on February 23, 2004 followed the procedures set forth in the specification and confirmed the screening utility set forth therein. The Examiner, in contrast, has provided no reason for doubting the asserted utility, and has provided no factual basis for believing that any of Applicants/Appellants' utilities would not be substantial and specific to the claimed invention.

Based on the arguments set forth, Applicants/Appellants submit that under the Standard of Rejection under 35 USC § 101, the Examiner has not met the burden of presenting a *prima facie* case that the claimed invention lacks patentable utility by providing evidence showing that one of ordinary skill in the art would reasonably doubt the utility asserted in the specification. Even if the Board considers that the Examiner has met this initial burden, Applicants/Appellants submit that sufficient rebuttal evidence has been provided to convince one of skill in the art of that the asserted utility was specific, substantial, and well-established such that the utility requirement under 35 USC § 101 has been satisfied.

A2. Enablement under 35 USC § 112, first paragraph

In OA 11/20/03, the Examiner rejected claim 1 under 35 USC § 112, first paragraph as allegedly not enabling one skilled in the art how to use the claimed invention "since the invention is not supported by either a specific and substantial asserted utility or a well-established utility." The rejection of Claim 1 under 35 USC § 112, first paragraph (enablement) was maintained in OA 5/19/04.

[2] "Further, sodium phosphate co-transporter family to which the polypeptide of SEQ ID NO:1 belongs is a family in which the members have ***divergent functions*** based on which tissues the protein is expressed or administered to.

B2. Standard of Rejection under 35 USC § 112, first paragraph (enablement)

Section 112, first paragraph, requires that the specification teach one of ordinary skill in the art how to make and use the invention. As stated by the court in In re Marzocchi (CCPA 1971) 439 F.2d 220, 169 USPQ 367:

> "[A] specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enablement requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support." (439 F.2d at 223, 169 USPQ at 369.)

C2. Application of Standard of Rejection under 35 USC § 112, first paragraph (enablement) to Claim 1

The Examiner's rejection under 35 USC § 112, first paragraph was based solely on the utility rejection under 35 USC § 101. From the arguments set forth in Section VIII C1 above, Applicants/Appellants submit that the Examiner did not meet the burden of presenting a *prima facie* case that the claimed invention lacks patentable utility by providing evidence showing that one of ordinary skill in the art would reasonably doubt the utility asserted in the specification. Therefore Claim 1 satisfies the utility requirement of 35 USC § 101.

Applicants/Appellants also assert that Claim 1 satisfies the enablement requirement of 35 USC § 112, first paragraph since the specification would have taught one of ordinary skill in the art how to make and use the invention at the time of filing. The amino acid sequence of the Npt2B polypeptide, as disclosed in Figure 1 and in SEQ ID NO:1, would enable the artisan to generate antibodies which can modulate the activity of Npt2B to treat specific diseases of phosphate metabolism. Methods of preparing such antibodies

---

Assignment to this family does not support an inference of utility because the members are not known to share a common utility." (OA 11/20/93 page 11 lines 17-21, emphasis added)

are described in the specification starting from page 21 line 3 to page 23 line 12. Also following the procedures described in the specification in Experimental Section B (page 29 line 23 to page 30 line 19), would enable the artisan to express the Npt2B polypeptide and perform screening assays to identify Npt2B modulatory agents useful for the treatment of diseases of phosphate metabolism. Furthermore, the figures and data contained in the Declaration of Suryanarayana Sankuratri which were obtained by following the procedures in Experimental Section B and which confirmed both the asserted activity and utility of the claimed invention, both demonstrate and prove that the specification was enabling at the time of filing.

D. Conclusion

The Examiner has failed to establish a *prima facie* showing that the asserted utility for Claim 1 is not specific or substantial. Applicants/Appellants have also provided evidence showing that the asserted utility for the present invention was well-established at the time of filing. Applicants/Appellants have also shown that the specification was fully enabling at the time of filing. Applicants/Appellants have therefore demonstrated that Claim 1 satisfies the utility requirement of 35 USC § 101 and the enablement requirement of 35 USC § 112, first paragraph. Accordingly, Applicants/Appellants request that the Board of Patent Appeals and Interferences reverse the rejection of Claim 1 on the grounds set forth herein.

Respectfully submitted,

David J. Chang, Ph.D.
Reg. No. 50,374

Roche Palo Alto LLC
Patent Law Dept. M/S A2-250
3431 Hillview Avenue
Palo Alto, CA 94304

Direct Phone: (650) 855-5316
Facsimile: (650) 855-5322
Date: October 12, 2004